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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/752,731	01/03/2001	Lawrence Loomis		1252

7590 07/26/2004

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EXAMINER	
PRATS, FRANCISCO CHANDLER	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/752,731	LOOMIS ET AL.	
	Examiner	Art Unit	
	Francisco C Prats	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60 and 65-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60 and 65-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4-28-2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1651.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 4, 2003, has been entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

It is noted that, in the submission of December 4, 2003, applicant requests an interview in this application. In view of the Art Unit change, and the shift in the pending grounds of rejection, applicant is requested to telephone the examiner at the number listed below if an interview is still desired.

Claims 60 and 65-81 are pending and are examined on the merits.

Information Disclosure Statement

The Information Disclosure Statement filed April 28, 2003, has been reconsidered, as requested by applicant in the submission of December 4, 2003. The non-patent literature lined through on the previous PTO Form 1449 has been found in a related case. A second copy of the previously filed PTO Form 1449 is supplied herewith. The previously non-considered non-patent literature has been considered and the PTO Form 1449 initialed to indicate that consideration. Previously considered prior art has been lined through. The PTO Form 1449 is supplied herewith.

Technically, it is improper for applicant cite numerous non-patent literature references on a PTO Form 1449, and fail to provide copies of the cited prior art, without providing a specific serial number for the application which contains the cited prior art. In the instant case, as applicant is aware, applicant has numerous copending applications, as well as numerous patented applications and abandoned applications. The file wrappers of most of these applications do not have copies of the cited non-patent literature documents within them. Thus,

by failing to specifically state the serial number of the application which contains copies of the cited documents, applicant in effect fails to provide copies of the references, since virtually all applicant's previous applications must be viewed to determine whether they contain the cited prior art.

Claim Rejections - 35 USC § 112

Claims 73-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 73 and 74 recite "further" process steps of administering a certain amount of enzyme units to a nasal or oral passage. These additional process steps do not make sense, given the fact that previous claim 60 is a product claim and cannot contain any actual positive process steps.

Similarly, claims 75-77 recite the process steps of administering the enzyme-containing therapeutic agent of claim 60 intravenously (claim 75), intramuscularly (claim 76) or subcutaneously (claim 77). This additional process step does not make sense, given the fact that previous claim 60 is a product claim and cannot contain any actual positive process steps.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 60 is rejected under 35 U.S.C. 102(b) as being anticipated by Gasson (EP 0 510 907 A2).

Claim 60 recites a composition comprising (1) a phage-encoded lytic enzyme specific for *Clostridium* and (2) a carrier suitable for parenteral delivery of the enzyme. Gasson describes a composition comprising a lytic enzyme specific for *Clostridium tyrobutricum* (see page 2, lines 16-18), said composition being suitably added to "water" (see page 2, line 58), which is a suitable parenteral carrier. The enzyme may also be combined with topical carriers in the form of a lotion cream or ointment (page 3, lines 4-6), which also may be administered parenterally, for example subcutaneously. It is noted that the described compositions are not *per se* intended for parenteral administration, as recited in applicant's claims. However, a recitation of the intended use of the claimed

invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case Gasson's water-containing enzyme composition as well as the topical compositions can be administered parenterally. A holding of anticipation is therefore required.

Note that this ground of rejection could be overcome by deleting the recitation "lytic enzymes" at line 5 of claim 60.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 60 and 65-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gasson (EP 0 510 907 A2).

As discussed above, because claim 60 encompasses a combination comprising "lytic enzymes" and a parenterally suitable carrier, Gasson anticipates claim 60. Gasson differs from the claims in not describing a single discrete embodiment where the *Clostridium* enzyme is combined with buffer, reducing agent (such as DTT), bacteriostat or chelating agent, as recited in claims 65-72. However, in view of the fact that Gasson discloses the utility of the enzyme as a testing agent for the target organism, one of ordinary skill would have been motivated to have combined the claimed buffers and chelating agents to have ensured the proper pH for the enzyme's activity. Similarly, to prevent degradation of the enzyme over time, one of ordinary skill would have been motivated to have included a reducing agent so as to ensure enzyme stability and prevent degradation of the enzyme. Lastly, the presence of a

bacteriostat would have been obvious in view of the fact that such an agent would have been recognized as being suitable for preventing undesirable proteins in Gasson's enzyme preparation. Thus, because Gasson provides motivation for combining the claimed ingredients, a holding of obviousness is required.

Note again that this ground of rejection could be overcome by deleting the recitation "lytic enzymes" at line 5 of claim 60

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 60 and 65-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,264,945. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the patented process claims of U.S. Pat. 6,264,945 include a recitation of the same product as recited in the claims under examination. In particular see claim 5 of the '945 patent. A terminal disclaimer is clearly required.

Claims 60 and 65-81 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent Nos. 6,264,945 in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793).

As discussed above, U.S. Patent No. 6,264,945, renders obvious certain the embodiments recited in the claims under examination. However, the '945 patent does not recites the use of shuffled or chimeric enzymes in the claimed compositions. However, each of Witte and Stemmer demonstrates not only that chimeric and/or shuffled enzymes were known in the art, but also that chimeric and/or shuffled enzymes possessed advantages when compared to their non-recombinant counterparts. Specifically, Witte demonstrates that the E-L chimeric lytic enzymes disclosed therein possess the lytic activities of both of the parent enzymes, as opposed to single activities possessed by the parent enzyme molecules. See Table 1, on page 160. Moreover, note the

extremely quick onset of lethality (1 minute) possessed by the chimeric protein made by the pRM1/3 plasmid, as compared to the parent enzymes (10 minutes and 20 minutes).

Further still, Stemmer demonstrates that enzyme shuffling results in enzymes having increased enzymatic activity. See e.g., column 9, lines 39-45. See also column 20, lines 12-15, discussing a 2 to 3 fold increase in beta lactamase activity resulting from shuffling. Thus, the artisan of ordinary skill, recognizing the advantages of using chimeric and/or shuffled enzymes, clearly would have been motivated to have used chimeric and/or shuffled enzymes in the compositions recited in the cited patents. A terminal disclaimer over the cited patent is clearly required.

Claims 60 and 65-81 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of U.S. Patent No. 6,264,945 in view of Witte et al (FEMS Microbiology Letters 164:159-167 (1998)) and Stemmer (U.S. Pat. 5,605,793), as discussed above, and in further view of Diaz et al (Molecular Microbiology 19(4):667-681 (1996)).

As discussed above, U.S. Patent No. 6,264,945, when viewed in light of Witte and Stemmer, is considered to render certain

of the claimed embodiments obvious. Neither the '945 patent nor Delisle/Witte/Stemmer disclose the use of a combination of holin and lysin enzymes, as recited in the claims. However, Diaz clearly discloses that the combined activity of holins and lysins provides optimal lysis of bacterial cells, when compared to holins or lysins alone. See, e.g., page 671, right column. ("Simultaneous expression of *ejh* [i.e., holin] and *ejl* [i.e., lysin] (Fig. 4F,L) showed the strongest and fastest (already observed after 60 minutes of induction) impact on cell morphology . . . .") Thus, the artisan of ordinary skill clearly would have been motivated to have added a holin enzyme to the lysin enzyme of U.S. Patent No. 6,264,945, in order to ensure optimal lysis of target pathogenic bacteria. A terminal disclaimer over the cited patent is therefore clearly required.

Claims 60 and 65-81 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application Nos. 09/908,737 and 09/844,435.

The claims of application serial number 09/908,737, directly recite a parenteral "agent" (i.e., a product), which contains one of the same therapeutic agent ingredients recited in the claims under examination. Thus, although the subject

matter recited in the copending applications is not of identical scope, a terminal disclaimer is clearly required because the copending sets of claims recite the same therapeutic agent in combination with the carriers suitable for the same purpose.

The '435 application contains process claims reciting, at their broadest, compositions containing a *Clostridium* lytic enzyme and a carrier, along with buffers and other excipients. See, e.g. claim 135 of the '435 application. A terminal disclaimer is clearly required.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 571-272-0926. The fax phone number for the

organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Francisco C Prats
Primary Examiner
Art Unit 1651

FCP